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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE, WA 98104-7092

EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	11

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,455	CHEN ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6, 7, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 9 is acknowledged.

Claims 9-22 and 25 have been cancelled as requested in the amendment of Paper No. 9, filed on March 04, 2003.

Claims 1-8, 23 and 24 are under examination in the instant office action.

Priority

2. Benefit of priority claimed under 35 U.S.C. 119(e) should either appear as the first sentence of the specification following the title, preferably as a separate paragraph or in an application data sheet, which is the instant situation.

Sequence compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence listing has been provided which includes the amino acid sequence presented in Figure 3 (transmembrane domains). In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of

the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

Furthermore, it appears that Figure 4 contains five amino acid sequences, while the description of the drawings identifies only four ("SEQ ID NOs: 4-7", page 8, line 20-21). Applicant is advised to clearly identify all the sequences presented in Figure 4, so that the name of each protein can be matched with the corresponding sequence identifier.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see page 96, line 21, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

5. The use of the trademarks has been noted in this application, see page 62, line 20, for example. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. It appears that Tables 1 and 3 and Tables 2 and 4 are identical. It is suggested that the second copy of each table is deleted in order not to duplicate information. If Applicant adopts this suggestion a substitute specification will be required..

Claim Objections

7. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 3 depends from claim 1, which is limited to a nucleic acid encoding a protein, while claim 3 encompasses a compliment of the nucleic acid encoding a protein. Therefore, claim 3 can be infringed by a nucleic acid, which does not infringe claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim. In the instant case, the complementary nucleic acid claim could be infringed without infringing the claims from which it depends. Therefore, it is improperly dependent and should be rewritten in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 13. Claims 3-8 depend from claim 1. However, the instant specification fails to describe the entire genus of nucleic acids, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecules of SEQ ID NO: 1 and 3, which encode a polypeptide of SEQ ID NO: 2, and of a nucleic acid molecule of SEQ ID NO: 12, which encodes a polypeptide of SEQ ID NO: 13. The subject matter, which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed to a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 13. First, the claims are not limited to a polynucleotide with a specific nucleic acid sequence. The claims only require the polynucleotide to share some degree of structural similarity to the isolated nucleic acids of SEQ ID NOs: 1, 3 or 12. The specification only describes polynucleotides having the nucleic acid sequences of SEQ ID NOs: 1, 3 and 12

and fails to teach or describe any other polynucleotide which lacks these specific nucleic acid sequences and encodes the polypeptide, which has the activities possessed by the isolated protein of SEQ ID NO: 2 or 13. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the prior art.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims except for the nucleic acids of SEQ ID NOs :1, 3 or 12. The specification does not provide a complete structure of those polypeptides which encode a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 13. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus, such as those nucleic acid molecules which encode a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 13. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. Claims 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 23 is directed to a composition comprising a pharmaceutically effective amount of the nucleic acid molecule of SEQ ID NO: 1 or 12, and claim 24 is directed to a composition comprising a pharmaceutically effective amount of an antisense oligonucleotide capable of hybridizing to the nucleic acid molecule of SEQ ID NO: 1 or 12. Thus, claims 23 and 24 recite language, such as "pharmaceutically effective amount", of intended use of the polynucleotides of the instant invention. However, the instant specification fails to provide enough guidance for one skilled in the art on how to practice the instant invention, thereby requiring undue experimentation to discover how to use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention is the demonstration that novel ATP Binding Cassette (ABC) transporter protein ABCG4 is capable of transporting molecules such as Aβ amyloid protein

across cell membranes (see page 1, last paragraph going to page 2, first paragraph of the instant specification and also results on pages 95-96 and Figures 7-9). It is suggested in the instant specification that the "[t]he ABCG4 transporter molecules of the present invention are useful as targets for developing modulating agents to regulate a variety of cellular processes, particularly the transport of neurotoxic molecules" (page 1, last paragraph going to page 2, first paragraph). However, the instant specification fails to provide any information regarding clinical administration of nucleic acids of the instant invention in a "pharmaceutically effective amount". The state of the art of administration of polynucleotides to a subject in general is considered being extremely unpredictable, and there is no known disclosure of routinely practiced administration of nucleic molecules for a desired clinical effect.

To practice an invention related to a composition comprising a pharmaceutically effective amount of a polynucleotide would require knowledge of the route, duration and quantity of administration of that nucleic acid molecule to a subject and this information is not provided by the instant specification. The text of the instant specification clearly fails to supply the guidance that would be needed by a routine practitioner. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual, of the claimed method. In the absence of this guidance a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of the nucleic acid molecule of SEQ ID NO: 1 or 12 or an antisense molecule of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in *In re Colianni*, 195 U.S.P.Q.

150,(CCPA 1977), which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

Thus, Applicant's invention is predicated on the finding that the instant claimed nucleic acid molecules encode ABCG4 polypeptide, which is capable of transporting molecules such as Aβ amyloid protein across cell membranes. Applicant further extrapolates this result into a composition comprising a pharmaceutically effective amount of the nucleic acid encoding ABCG4 or corresponding antisense nucleic acid. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine amount of the nucleic acid encoding ABCG4 for use as pharmaceuticals, as well as routes and regime of administration.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the

enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for a composition comprising a pharmaceutically effective amount of the nucleic acid molecule of SEQ ID NO: 1 or 12 or an antisense nucleotide hybridizing to the nucleic acid molecules of SEQ ID NO: 1 or 12. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-8 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 1 is vague and indefinite for recitation "allelic variant binds to an antibody that selectively binds to the polypeptide of SEQ ID NOs: 2 or 13", emphasis added. The metes and bounds of the limitation "selectively binds" cannot be determined from the claim or the instant specification. Moreover, if the selectivity of the recited antibody is limited to recognizing only

the polypeptides of SEQ ID NO:s 2 or 13, then it appears that it cannot bind to an allelic variant, which lacks these sequences. Clarification is required.

12. Claim 6 is vague and indefinite because it depends from itself. For the purpose of the examination claim 6 is interpreted as being dependent from claim 5.

13. Claim 24 is indefinite and ambiguous for recitation "specifically hybridizing ". It is not clear what process or what conditions of hybridization are to be included or excluded in order to meet the limitation "specific". Moreover, Applicant is advised that without providing a precise set of hybridization conditions, in the claim or the specification, the metes and bounds of the claimed isolated nucleic acid molecule cannot be defined.

14. Claims 2-5, 7 and 8 are indefinite for being dependent from the indefinite claim.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
June 27, 2003